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DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
ROYDS, LESLIE A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,697	COUCH ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and submission filed August 15, 2007 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Claims 1-28 are pending and under examination. Claims 1 and 16 are amended.

It is noted for the record that the Examiner has fully and carefully considered Applicant's remarks presented at pages 7-8 of the Amendment filed August 15, 2007. In response thereto, a rejection under 35 U.S.C. 112, first paragraph, written description, rejection is set forth below to address the limiting effect of the claimed limitation directed to "wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day".

Applicant's arguments, filed August 15, 2007, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 101 (New Grounds of Rejection)

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 22-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-

statutory subject matter.

Present claim 22 is directed to the pharmaceutical combination of claim 1, which is a pharmaceutical combination comprising an effective amount for a day of l- and d-amphetamine, each in base and/or salt form, and wherein the molar ratio of l-amphetamine to d-amphetamine released from the combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day, wherein doses are administered individually at different times or are administered once in a single staged-release dosage form.

Present claim 23 is also directed to the pharmaceutical combination of claim 1, wherein doses are administered in one or more dosage forms that are either immediate release or pulse release dosage forms and/or sustained or controlled release dosage forms. Present claim 24 depends from claim 23 and specifies that the sustained or controlled release dosage form or dosage forms contain the l isomer.

Present claim 25 is also directed to the pharmaceutical combination of claim 1, wherein two doses of amphetamine are administered to the patient in a day, the first dose having an l to d isomer ratio of about 1:3 or contains only d isomer, and the later dose having an l to d isomer ratio of greater than 1:1 or contains l isomer only. Present claim 26 depends from claim 25 and specifies that the second dose contains l isomer only.

Instant claims 22-26 are directed to non-statutory subject matter because the claims embrace two statutory categories of invention, i.e., both product and process. Specifically, claims 22-23 and 25 embrace the product limitations of claim 1, but then further recite limitations directed to the manner and process of administering doses of the claimed product. Furthermore, claims 24 and 26 are also directed to non-statutory subject matter as a result of their dependency from claims 23 and 25. Accordingly, it is unclear whether Applicant intends to claim a product or a process in instant claims 22-26. The overlap between these two statutory categories of invention (i.e., product and process) renders the subject matter of non-statutory under 35 U.S.C. 101 because 35 U.S.C. 101 is drafted in a manner so as to set forth the

statutory classes of invention *in the alternative only.* Please see *Ex parte Lyell*, 17 USPQ2d 1548 (Bd. Pat. App. & Inter. 1990) Id. at 1551.

For the purposes of examination and the application of prior art, instant claims 22-26 will be interpreted to read upon a product, not a process.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claim 1 (and the claims dependent therefrom) is directed to a pharmaceutical combination comprising an effective amount for a day of l- and d-amphetamines, each in base and/or salt form, and wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day. Present claim 28 is directed to the administration of the composition of present claim 1 for treating inattentiveness in a human ADHD patient.

Present claim 16 (and the claims dependent therefrom) is directed to a method for treating ADHD comprising administering to a human effective amounts of the l- and d-isomers of amphetamine, each independently in free base and/or salt form, and wherein the molar ratio of l-amphetamine to d-amphetamine administered in a time period later in the day is higher than the ratio administered in a time

period earlier in the day; the total amount of l-isomer to the total amount of d-isomer administered per day is greater than 1:3; and the time period later in the day is at least about one hour following the time period earlier in the day.

In particular, the specification and claims as originally filed fail to provide adequate written description for the limitation directed to the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day being higher than said ratio released therefrom in a time period earlier in the day under *any* conditions (claim 1).

MPEP §2163 states, "The issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not convention in the art or known to one of ordinary skill in the art...The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test of sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096

(Fed. Cir. 1983))...Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)."

Applicant's disclosure is replete with discussion of possible technologies that may be employed to affect the claimed release profile, i.e., wherein the molar ratio of l-amphetamine to d-amphetamine released from the combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day, but fails to provide specific details and/or written description of the particular structure (or structures, if appropriate) that may be employed to achieve the claimed function of the l- and d-amphetamine combination.

Applicant is reminded that rejections under the written description requirement of 35 U.S.C. 112, first paragraph, are set forth when the claim scope is not commensurate with what is disclosed, and, therefore, what was in possession of the Applicant at the time of the invention, in the accompanying specification. In the instant case, while generic technologies such as extended release tablets, pulsing techniques using enteric coatings, osmotic systems, layered bead formulations, immediate release formulations, etc., were technologies that could have been employed during manufacture of the pharmaceutical combinations to effect the claimed function, Applicant's specification clearly demonstrates that the skilled artisan would have been required to execute extensive testing and experimentation using a variety of different formulations (in fact, conceivably all of the various described technologies in the instant specification, in the absence of any guidance or direction as those formulations with a specific structure that would, at the very least, have been reasonably expected to function in the manner claimed), to determine if such formulations actually effected the release of a higher molar ratio of l-amphetamine to d-amphetamine in a time period later in the day than the ratio released therefrom in a time period earlier in the day.

It is this very need for testing amongst widely varying species of pharmaceutical formulation technology to determine the full scope of the types of formulations that may be used to actually effect release in the manner claimed that is clearly demonstrative of the fact that Applicant was not in possession of the full scope of subject matter presently claimed, since the instant claims read upon the use of *any* formulation to achieve the claimed function without describing with significant particularity those *specific* types of formulations or the structure(s) that are responsible for the claimed function. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention." Please reference MPEP §2163.

Applicant further discloses various "examples" of pharmaceutical combinations at pages 34-39. However, it is noted that the combinations described in Example 6 are generic to non-specific types of pharmaceutical formulation, such as, e.g., multi-laminated beads, delayed-release beads, delayed-release tablets, osmotic tablets with a blank layer, etc., wherein the particular elements of these formulations that would be considered essential for achieving the claimed function are not sufficiently described such that the skilled artisan would have been able to readily envision the structure and/or elements responsible for the particular function claimed. Additionally, though Examples 7-10 do, in fact, specify particular elements of the composition and a manner of making the exemplified composition, the disclosure and examples are devoid of any explanation as to how these particular exemplified compositions operate to achieve the claimed function in such a manner that the skilled artisan would have recognized that these specific compositions were capable of functioning in the manner claimed.

Despite this disclosure of these "examples" and the *concept* of a pharmaceutical combination of l- and d-amphetamine wherein the molar ratio of l-amphetamine to d-amphetamine released from the

pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day, Applicant has failed to describe, with significant particularity, the structure, material or acts that are responsible for effecting the function of the combination as claimed. Though the disclosure is replete with various technologies that *may be used* for this purpose, Applicant is very clearly imposing the burden of extensive testing upon the skilled artisan to identify the particular technologies, structure, elements, formulations, etc. that may effect the claimed function, but which Applicant has not identified and, thus, was not in possession of, at the time of the present invention.

It has been held in patent law that a wish or plan for obtaining the invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004). In other words, though Applicant may have a *plan* for how to formulate the claimed combination of l- and d-amphetamine for use in the present invention, it remains that *at the time of the invention*, Applicant had not identified such specific formulations, and, therefore, did not have written description of the full scope of subject matter now claimed.

Further, though Applicant has attempted to limit the claimed combination to that which performs this particular function, e.g., those combinations wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day, it remains that Applicant has not appropriately defined the metes and bounds of the claim when limited by this function. Adequate description of a functional step may be provided if the written description adequately links or associates an adequately described *particular structure, material, or act to the function* or if it is clear *based on the facts of the application that one skilled in the art would have known what structure, material, or acts would perform the function.* The instant application does not meet either of these criteria. The present

specification provides no disclosure beyond the generic disclosure of the required function that would correlate a common structural element or material to performance of the claimed function and that would be readily identifiable to one of skill in the art.

Lastly, the instant disclosure cites a number of publications, foreign patents, etc. in the discussion of the various pharmaceutical technologies that may be employed. Applicant is notified that reliance upon any of these documents for a description of essential subject matter and/or to overcome the instant rejection would be considered an improper incorporated by reference. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. If Applicant were to rely upon such subject matter, Applicant would be required to amend the disclosure to include the material incorporated by reference, if the material was relied upon to overcome any objection, rejection, or other requirement imposed by the Office. Such an amendment would require a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. Please see 37 C.F.R. 1.57(f).

Accordingly, for these reasons described *supra*, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claim 16 is directed to a method for treating ADHD comprising administering to a human effective amounts of the l- and d-isomers of amphetamine, each independently in free base and/or salt form, and wherein the molar ratio of l-amphetamine to d-amphetamine administered in a time period later

in the day is higher than the ratio administered in a time period earlier in the day; the total amount of l-isomer to the total amount of d-isomer administered per day is greater than 1:3; and the time period later in the day is at least about one hour following the time period earlier in the day.

In particular, the specification and claims as originally filed fail to provide adequate written description for the limitations directed to the time period later in the day being at least about one hour following the time period earlier in the day (claim 16).

MPEP §2163 states, "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test of sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))...Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)."

Regarding Applicant's newly added limitations, Applicant directs the Examiner to the instant specification at page 2, line 31-page 3, line 1; page 3, lines 20-23; and page 5, line 13-page 6, line 13 in

support of the claim amendments. Relevant disclosure was found at, for example, page 5-6, which states:

"More of the l-isomer can be administered than currently in Adderall XR® and/or in Adderall® immediate-release tablets in a given day and/or in at least one dose; e.g., where two or three doses are pulsed or otherwise administered per day (e.g., 1-6 hours apart, preferably 2-4 hours apart, as described in, e.g., WO 00/23055), additional l-isomer can be administered separately or within one or more of the administered doses such that the total daily amount of l-isomer is increased; the amount of l-isomer in each of the usual Adderall XR® or immediate-release tablet doses or pulses can be increased by including additional l-isomer in each component of the dosage form. (The weight ratio of d- to l-isomer in these Adderall® products is precisely known from the published amounts of each amphetamine salt in Adderall®, e.g., as in the package insert for Adderall®, immediate release.)"

While such teachings have been fully and carefully considered, it is noted that such disclosure fails to be supportive of the concept of, specifically, the time period later in the day being at least one hour following the time period earlier in the day. The disclosure of the administration of two or three doses per day, such as one hour apart, of the l-isomer fails to provide adequate written support to now narrow the claims to read specifically upon the separation of the time period earlier in the day from the time period later in the day by at least about one hour. This is because the context in which Applicant discloses the separation of dose administration by one hour is clearly directed to the administration of the doses containing more l-isomer (i.e., those that are administered later in the day), wherein multiple doses of this l-isomer (or at least l-isomer enriched product) may be separated by 1-6 hours, preferably 2-4 hours. This represents a narrowing of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure. It is clear, therefore, that Applicant was not in possession of the concept of the time period later in the day being at least about one hour following the time period earlier in the day.

Furthermore, assuming *arguendo* that this cited portion of the disclosure did provide adequate

written description to support this newly added limitation of instant claim 16, which the Examiner does not concede, it is noted that the disclosure of a one hour difference between the time period earlier in the day and the time period later in the day would clearly fail to provide adequate written support to now broaden the claims to read upon "at least about one hour" difference between the two time periods. This would represent a clear broadening of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately support, either explicitly or implicitly, by the original disclosure because the disclosure of a specific time period, i.e., one hour, does not suggest variation above or below the set time period, whereas the use of the word "about" is clearly indicative of variation around the time period disclosed.

As stated in MPEP §2163, "The subject matter of the claim need not be described literally (i.e., using the same terms of *in haec verba*) in order for the disclosure to satisfy the description requirement." However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the concept of the time period later in the day being at least about one hour following the time period earlier in the day (claim 16).

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11, 14-15 and 22-24 remain rejected under 35 U.S.C. 102(b) as being anticipated by Burnside et al. (U.S. Patent No. 6,322,819; 2001), already of record, for the reasons of record set forth at pages 4-7 of the previous Office Action dated May 16, 2007, of which said reasons are herein incorporated by reference.

Claims 1-15 and 27-28 remain rejected under 35 U.S.C. 102(b) as being anticipated by Patrick et al. ("Pharmacology of Methylphenidate, Amphetamine Enantiomers and Pemoline in Attention-Deficit Hyperactivity Disorder", 1997; p.527-546), already of record, for the reasons of record set forth at pages 5-7 of the previous Office Action dated May 16, 2007, of which said reasons are herein incorporated by reference.

Applicant traverses the rejection over Burnside et al. and the rejection over Patrick et al., stating that the recited release ratio is limiting on the instant claims and, since cited reference fail to teach the recited release ratio, the claims are not anticipated and the rejection should be withdrawn.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

In response thereto, Applicant is reminded that the instant claims, as presently written, fail to set for the particular structure(s), material(s) or act(s) that are responsible for the pharmaceutical combination to function in the manner claimed (i.e., to release a molar ratio of l-amphetamine to d-amphetamine in a time period later in the day that is higher than the ratio released therefrom in a time period earlier in the day). Applicant's attention is directed above to the discussion presented under 35 U.S.C. 112, first paragraph, which describes the reasons behind this assertion.

In view of this fact, Applicant's failure to explicitly set forth the physical structure(s), material(s) or element(s) *in the claims* that are essential to effecting the claimed function (or even to adequately describe it in the accompanying specification) is clearly indicative of the fact that the claims *per se* fail to distinguish themselves over a physical and structural combination of both l-amphetamine and d-

amphetamine, each in base and/or salt form. Despite the recited release profile of the claimed combination, the claims do not specify the particular structural elements responsible for this function and, therefore, the claimed release of the composition fails to patentably limit the actual physical combination of both l- and d-amphetamine, since the only required physical components of the claimed combination are the l- and d-amphetamines, each in base and/or salt form.

Accordingly, it is properly maintained herein that the claimed function directed to "wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day" is not patentably limiting to the claimed pharmaceutical combination. In light of this fact, the claims remain properly rejected over the prior art of record, further relying upon the guidance provided at MPEP §2112.01, which states, "Where the claimed and prior art products are identical or substantially identical *in structure or composition*, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established...Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. *Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present.*" (emphasis added)

For these reasons described *supra*, and those previously made of record at pages 4-7 of the previous Office Action dated May 16, 2007, rejection of claims 1-11, 14-15 and 22-24 over Burnside et al. or the rejection of claims 1-15 and 27-28 over Patrick et al. each remain proper and are **maintained**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Patrick et al. ("Pharmacology of Methylphenidate, Amphetamine Enantiomers and Pemoline in Attention-Deficit Hyperactivity Disorder", 1997; p.527-546) in view of Epstein et al. (WO 2002/039998; 23 May 2002), Burnside et al. (U.S. Patent No. 6,322,819; 2001), STN Registry File (Registry No. 156-34-3) and Tulloch et al. ("SLI381 (Adderall XR), a Two-Component, Extended Release Formulation of Mixed Amphetamine Salts: Bioavailability of Three Test Formulations and Comparison of Fasted, Fed and Sprinkled Administration, *Pharmacotherapy*, 2002; 22(11):1405-1415), each already of record, for the reasons of record set forth at pages 7-10 of the previous Office Action dated May 16, 2007, of which said reasons are herein incorporated by reference.

Applicant traverses the instant rejection, stating that the claims now specify that the molar ratio of l-amphetamine to d-amphetamine administered in a time period later in the day is higher than the ratio administered in a time period earlier in the day and that the time period later in the day is at least about one hour following the time period earlier in the day. Applicant alleges that the cited references fail to teach this release pattern and, therefore, the rejection should be withdrawn. Applicant further alleges that none of the prior art, whether alone or in combination, discloses or suggests increasing the release ratio of l- to d-amphetamine as the day progresses and, further, that the prior art does not provide the motivation

to one of ordinary skill in the art to vary the l- to d- release ratio as the day progresses in the claimed manner. Still further, Applicant submits that Epstein teaches away from the instant claims because there is no motivation in Epstein to administer any d-amphetamine.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

In response thereto, Applicant is reminded that the instant claims, as presently written, fail to set for the particular structure(s), material(s) or act(s) that are responsible for the pharmaceutical combination to function in the manner claimed (i.e., to release a molar ratio of l-amphetamine to d-amphetamine in a time period later in the day that is higher than the ratio released therefrom in a time period earlier in the day). Applicant's attention is directed above to the discussion presented under 35 U.S.C. 112, first paragraph, which describes the reasons behind this assertion.

In view of this fact, Applicant's failure to explicitly set forth the physical structure(s), material(s) or element(s) *in the claims* that are essential to effecting the claimed function (or even to adequately describe it in the accompanying specification) is clearly indicative of the fact that the claims *per se* fail to distinguish themselves over a physical and structural combination of both l-amphetamine and d-amphetamine, each in base and/or salt form. Despite the recited release profile of the claimed combination, the claims do not specify the particular structural elements responsible for this function and, therefore, the claimed release of the composition fails to patentably limit the actual physical combination of both l- and d-amphetamine, since the only required physical components of the claimed combination are the l- and d-amphetamines, each in base and/or salt form.

Accordingly, it is properly maintained herein that the claimed function directed to "wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day" is not patentably limiting to the claimed pharmaceutical combination. In light of this fact, the claims remain

properly rejected over the prior art of record, further relying upon the guidance provided at MPEP §2112.01, which states, "Where the claimed and prior art products are identical or substantially identical *in structure or composition*, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established...Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. *Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present.*" (emphasis added)

In view of the non-limiting nature of these limitations, instant claim 16, directed to a method for treating ADHD, solely requires the administration of effective amounts of the l- and d-isomers of amphetamine, each independently in free base and/or salt form, wherein the total amount of l-isomer to the total amount of d-isomer administered per day is greater than 1:3 (claim 16) and wherein a further embodiment specifies the administration of two doses to the patient, with one dose having an l to d isomer ratio of about 1:3 or contains only d isomer and the later dose has an l to d isomer ratio of greater than 1:1 or contains l isomer only (claim 20). This is clearly suggested by the prior art teachings of Patrick et al. in view of Epstein et al. (see, e.g., p.12-13 of the Office Action dated October 20, 2006), which clearly teaches that the l-isomer of amphetamine was known to have enhanced efficacy and reduced side effects (i.e., addiction) and compositions of both the l-isomer (either enriched for l-isomer or containing l-isomer alone), as well as compositions of the l- and d-isomers with more d- than l-isomer, were both known in the art for the treatment of ADHD (see Patrick et al., p.536-538 and Epstein et al., p.16, l.6-15). Therefore, the administration of a combination of these two known compositions, in either order, would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention because each was known to be effective for the same therapeutic purposes and, thus, would have been expected to achieve additive, if not synergistic, ADHD-reducing effects when combined. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069.

Though Applicant opines that Epstein et al. teaches away from administering any d-amphetamine (Applicant's remarks, p.11), Applicant is reminded that Epstein et al. not only teaches compositions of (R)-amphetamine (i.e., equivalent to l-amphetamine; see also Epstein et al., p.26, l.26-32), but also teaches compositions of one or more amphetamine compounds that includes (R)-amphetamine (p.16, l.18-21), but may also comprise the use of a racemic amphetamine mixture (i.e., equal amounts of (R) and (S) isomers, equivalent to l- and d-isomers) or an amphetamine mixture enriched for one isomer over the other (p.27, l.1-11). This is a clear teaching that Epstein et al. does not limit his disclosure solely to the administration of l-amphetamine alone and very obviously contemplates the use and administration of the d-isomer also, wherein the quantities of each may be varied. In other words, the fact that Epstein et al. provides this teaching of the inclusion of d-amphetamine in the disclosed compositions is clearly indicative of the fact that the reference does not teach away from its use.

For these reasons described *supra*, and those previously made of record at pages 7-10 of the previous Office Action dated May 16, 2007, the rejection of claims 1-28 over Patrick et al. remains proper and is **maintained**.

Double Patenting

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 and 22-26 remain rejected under the judicially created doctrine of obviousness-type

double patenting as being unpatentable over the composition claims of U.S. Patent Nos. 6,605,300; 6,322,819; or 6,913,768, and remain provisionally rejected over the composition claims of U.S. Patent Application Nos. 11/091,011; 10/758,417; or 11/030,174, each already of record, for the reasons of record set forth at pages 10-11 of the previous Office Action dated May 16, 2007, of which said reasons are herein incorporated by reference.

Applicant is again reminded that the obviousness-type double patenting rejection over U.S. Patent Application No. 11/150,311 has been indicated as **withdrawn** at page 11 of the previous Office Action dated May 16, 2007 because the '311 application is no longer pending before the Office.

Applicant's request that the rejections be held in abeyance until allowable subject matter has been identified is noted.

In view of the fact that allowable subject matter has not been identified at the present time, and further in view of the fact that Applicant presents no arguments or Terminal Disclaimers regarding the obviousness-type double patenting rejections of record, the rejections remain proper for the reasons set forth at pages 10-11 of the previous Office Action and are, therefore, **maintained**.

Conclusion

Rejection of claims 1-28 remains proper and is **maintained**.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

November 8, 2007

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER